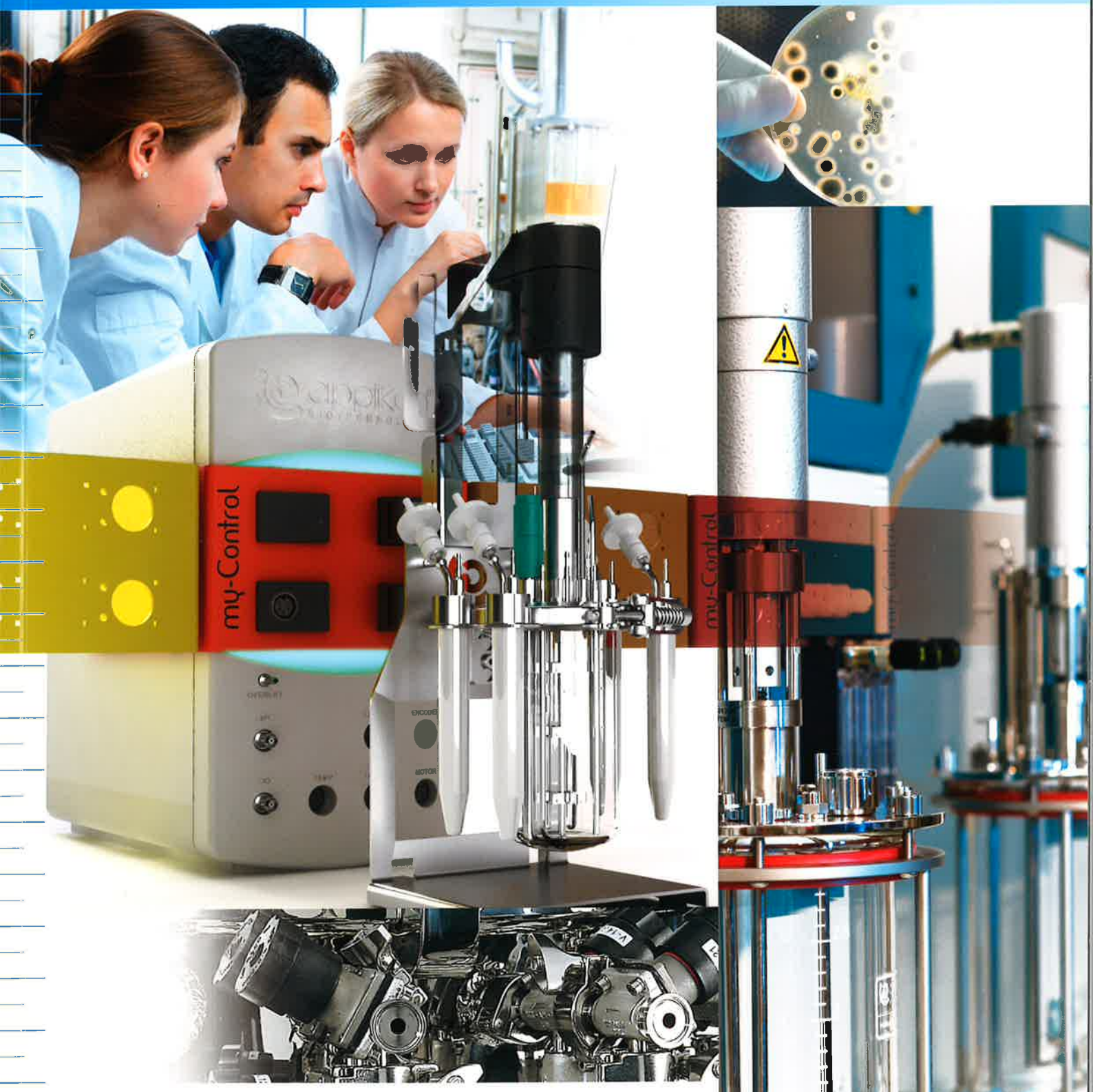
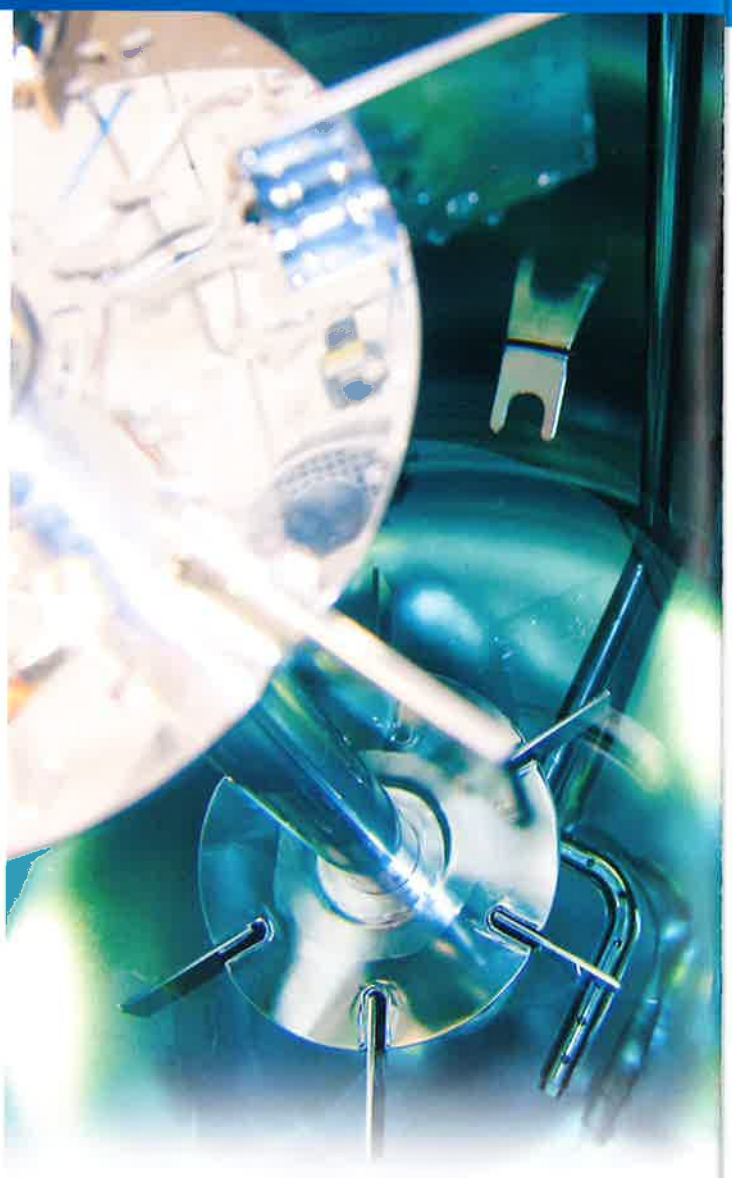


Cultivation Systems

From Discovery to Production

applikon® BIOTECHNOLOGY

a step ahead



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Applikon Biotechnology, a step ahead

Applikon Biotechnology is a world leader in developing and supplying advanced bioreactor systems from laboratory scale to production scale. We partner with our customers to implement scalable platforms from initial screening through development and full-scale production. This minimizes scale-up risks and guarantees the shortest time to market for our customers' new product development.

New technologies

Applikon is known for bringing new technologies to the market. These new technologies offer advantages in process efficiency for research and development as well as pilot plant and production scale processes.
Your advantage? Working with the latest technology offering a competitive advantage in efficiency and reliability.

Reliable

As a privately owned company our focus is on building a healthy company by supplying the best product offering for our customers now and in the long-term future. This is the basis of many long-term relationships with our clients all over the world.
Your advantage? Applikon can always support you through the well trained sales consultants and technicians of our technical support department.

High Tech

Applikon Biotechnology is unique in the mini and micro bioreactor range. No other company can offer this complete solution on a very small scale. We develop small scale systems to generate results that can be scaled to production scale. There are thousands of Applikon bioreactors used in the world from small scale R&D up to full scale cGMP production.
Your advantage? The best solution from micro scale to full scale production resulting in the shortest time to market for your new products.

Worldwide activities

Since we started in 1974 we have shown a healthy growth resulting in a global market leader role. R&D, design and engineering are in house in our headquarters in Delft, The Netherlands. We have our own sales and service organizations in the USA, the UK and China. We have well trained local distributors for sales and service in over 20 countries.
Your advantage? No matter where you are you can always rely on Applikon, now and in the future.

Our Mission

Providing reliable solutions for the bioprocess market that will enable an improved quality of life.

applikon® BIOTECHNOLOGY a step ahead

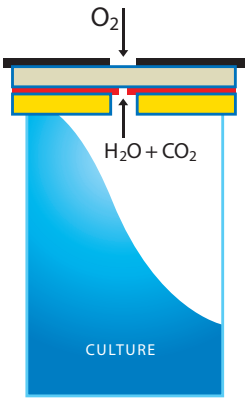
Micro-Flask by Duetz, cultivation in microtiter plates

The Micro-Flask system facilitates reproducible and reliable culturing on microtiter plates. The system consists of sandwich covers, cover clamps and cryo-replicator. The Micro-Flask enables a single person to grow and test thousands of strains simultaneously with a minimum of repetitive handling.

Cryo-Replicator for simple inoculation of 96-well microtiter plates

Features

- Conversion of 24 and 96 microtiter plates (both deep- and low-well plates) into individual micro-reactors
- Low and uniform evaporation rates for every well
- Sterile barrier for individual wells prevents cross contamination
- Oxygen transfer rates similar to shake flasks in standard orbital shakers
- Simultaneous and reproducible sampling of 96 frozen glycerol stocks



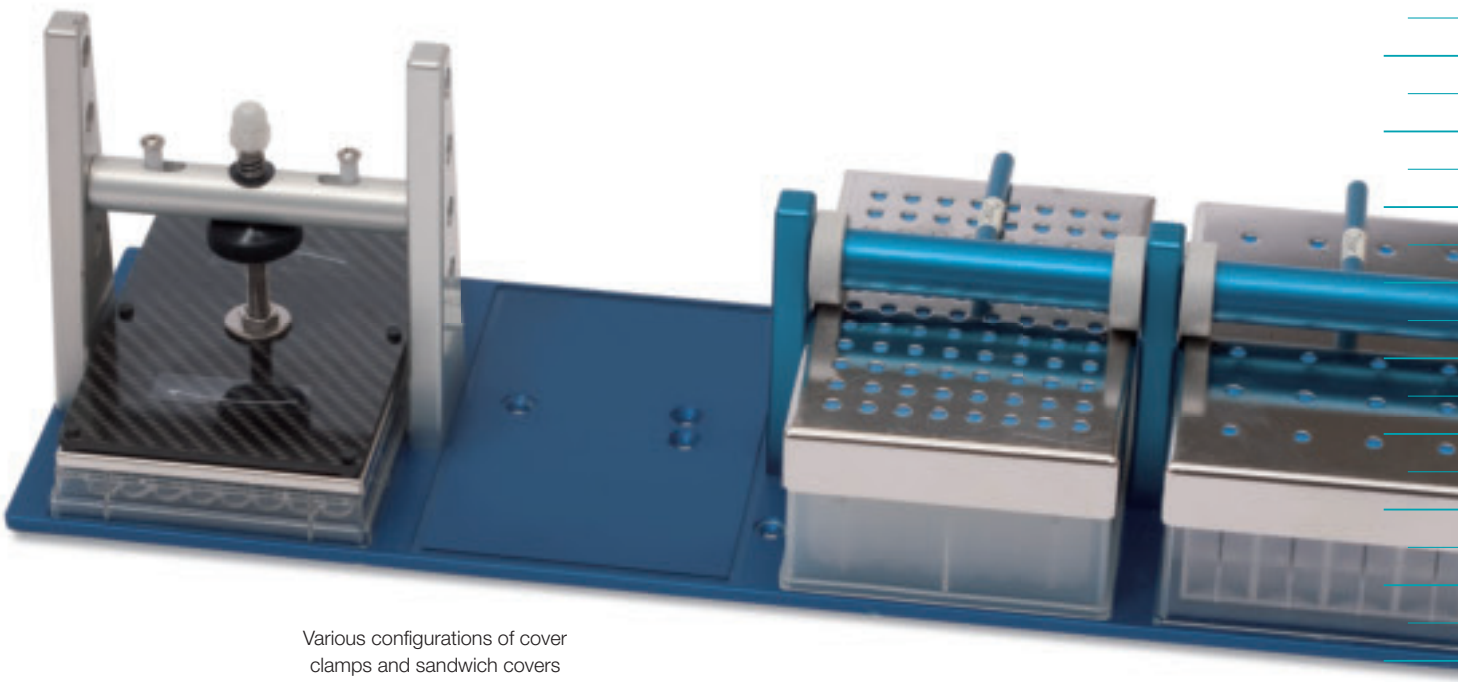
Cross-section of Micro-Flask sandwich cover

Applications

- High throughput screening and distribution of mutant and construct libraries e.g. in E. coli or yeast
- Metabolic flux studies and high-throughput screening for high activity prokaryotic or eukaryotic mutants
- Comparative studies, e.g. clinical isolates
- Growth medium optimization for cell lines or production strains

Specifications

Type of microtiter plate	Well volume	Culture volume	Orbital shaking frequency	Shaking amplitude	O_2-transfer rate (30˚C, air, 1 bar)	Headspace refreshment rate	Evaporation rate per well (at 30˚C)	Mixing pattern at 300 rpm ampl. 25 mm	Mixing pattern at 300 rpm ampl. 50 mm
24-square deep-well polypropylene, 17x17 mm, depth 40 mm	11000 µl	2500 µl 2500 µl 2500 µl 4000 µl 4000 µl	300 rpm 300 rpm 220 rpm 300 rpm 220 rpm	50 mm 25 mm 50 mm 50 mm 25 mm	51 mmol O_2 / l / h 39 mmol O_2 / l / h 35 mmol O_2 / l / h 24 mmol O_2 / l / h 24 mmol O_2 / l / h	2.5 ml / min (1 VVM) 2.5 ml / min (0.6 VVM)	**50% humidity:** 50 µl H_2O per day **75% humidity:** 25 µl H_2O per day	2500 µl	2500 µl
24-round low-well polystyrene, ∅ 16 mm, depth 18 mm	3000 µl	750 µl 750 µl 1000 µl 1000 µl	300 rpm 300 rpm 300 rpm 300 rpm	50 mm 25 mm 50 mm 25 mm	40 mmol O_2 / l / h 25 mmol O_2 / l / h 30 mmol O_2 / l / h 19 mmol O_2 / l / h	1.1 ml / min (1.4 VVM) 1.1 ml / min (1.1 VVM)	**50% humidity:** 30 µl H_2O per day **75% humidity:** 15 µl H_2O per day	1000 µl	1000 µl
96-square deep-well polypropylene, 8x8 mm, depth 40 mm	2400 µl	500 µl 500 µl 750 µl 750 µl 1000 µl 1000 µl	300 rpm 300 rpm 300 rpm 300 rpm 300 rpm 300 rpm	50 mm 25 mm 50 mm 25 mm 50 mm 25 mm	38 mmol O_2 / l / h 12 mmol O_2 / l / h 24 mmol O_2 / l / h 7 mmol O_2 / l / h 18 mmol O_2 / l / h 3 mmol O_2 / l / h	1 ml / min (2 VVM) 1 ml / min (1.3 VVM) 1 ml / min (1 VVM)	**50% humidity:** 22 µl H_2O per day **75% humidity:** 11 µl H_2O per day	750 µl	750 µl
96-round low-well polystyrene, ∅ 6.5 mm, depth 11 mm	380 µl	100 µl 100 µl 150 µl 150 µl 200 µl 200 µl	300 rpm 300 rpm 300 rpm 300 rpm 220 rpm 300 rpm	50 mm 25 mm 50 mm 25 mm 50 mm 25 mm	39 mmol O_2 / l / h 20 mmol O_2 / l / h 32 mmol O_2 / l / h 16 mmol O_2 / l / h 12 mmol O_2 / l / h 12 mmol O_2 / l / h	250 µl / min (2.5 VVM) 250 µl / min (1.7 VVM) 250 µl / min (1.3 VVM)	**50% humidity:** 6 µl H_2O per day **75% humidity:** 3 µl H_2O per day	150 µl	150 µl



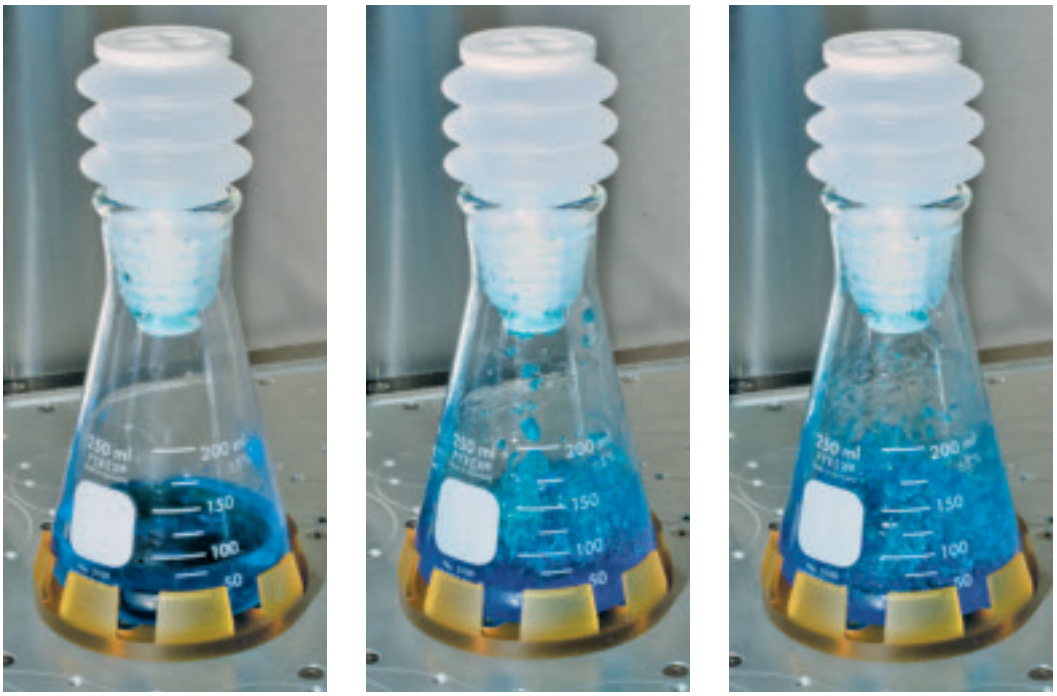
Various configurations of cover clamps and sandwich covers

RAMbio®, the high intensity mixer

The RAMbio® bench top biological mixer utilizes ResonantAcoustic® technology that applies low-frequency, high-intensity acoustic energy to agitate microbial cultures. The RAMbio® is a highly-efficient mixer/incubator that dramatically enhances oxygenation and bulk mixing for bacterial and fungal cultures. Combined with the patented Oxy-Pump® stopper, oxygen transfer rates up to 6-fold higher than orbital-shaken cultures can be achieved.

Features

- Increased oxygen transfer for aerobic cultures
- Rapid turnover of any desired gas
- Take advantage of richer media formulations
- 2-6 fold increase in plateau biomass levels
- Up to 10-fold increase in product expression
- Up to 6-fold increase in Oxygen Transfer Rate
- Up to 5 times shorter cultivation time
- Humidity control



Shake flask under the influence of ResonantAcoustics®

Specifications

Capacity	18 x 250 ml flasks or
	14 x 500 ml flasks or
	8 x 1000 ml flasks
Dimensions	102 x 57 x 70 cm (W/D/H)
	40 x 27 x 23”
Temperature control	Ambient +5°C to 60°C
Weight	200 kg (440 lbs)
Humidity control	Ambient to 90% RH
Power	110/230 VAC, 50/60 Hz
Mixing power	3 - 20g acceleration (196 m/sec^2)

Anaerobic Fermentation Monitor, simple parallel cultivation

The Anaerobic Fermentation Monitor (or AFM) is a robust and user-friendly laboratory parallel fermentation system that allows for accurate comparisons of carbon conversion rates and yields for six simultaneous anaerobic fermentations.
Monitoring the amount of gas that evolves from a fermentation broth under well controlled conditions is a reliable comparison method that has proven to be very useful in all industries that use anaerobic fermentations. Because carbon dioxide production is stoichiometrically coupled with carbon source conversion, very useful metabolic data can be obtained.
The AFM provides very accurate standard measuring of gas from six parallel fermentations that is both very low in maintenance and very easy to use.

Features

- Very user friendly laboratory device for monitoring anaerobic, metabolic yeast activity for alcohol production
- Six independent yeast fermentations can be carried out simultaneously
- Stirrer speeds and temperatures can be set or time programmed for each fermenter flask individually
- Accurate comparison of conversion rates and yields under different conditions such as temperature, strain type, carbon source or nutrients
- Much easier to operate and cleaner than standard fermenter systems
- Fully controlled with user-friendly PC control and data analysis software
- Automatic generation of advanced reports containing all measured data, data analysis tables and corresponding graphs
- Very strong magnetic stirrers, able to handle very viscous media
- Proven value for research and QA purposes in all fields of yeast research and (bio) ethanol production

Applications

- Measure conversion rates and yields of lignocellulose hydrolysates into biofuels
- Test and compare different yeast strains or different feedstock/substrates
- Quality control of regular/commercial yeast
- Quality control of traditional feedstock (such as molasses)
- Conversion of wort into beer
- Conversion of grape juice into wine
- Alcohol tolerance and toxicity studies
- Industrial and academic research on yeast and potable alcohol/bio-ethanol/bio-butanol production

Specifications

Total volume (liter)	6 reactors of 250 ml or 500 ml
Working volume (liter)	200 ml or 400 ml
Minimum working volume (liter)	50 ml or 100 ml
Drive system	Magnetically coupled drive
Maximum stirrerspeed (rpm)	Standard range is 50 - 500
Impellers	Marine type
Exhaust gas	Exhaust gas connection
Temperature	Measurement: Pt-100 sensor in central stirrer bar
	Control: heating via central stirrer bar
Dimensions (DxWxH)	30 x 85 x 67 (cm)
Empty Weight (kg)	75 kg

Mini bioreactors, real small... real bioreactors

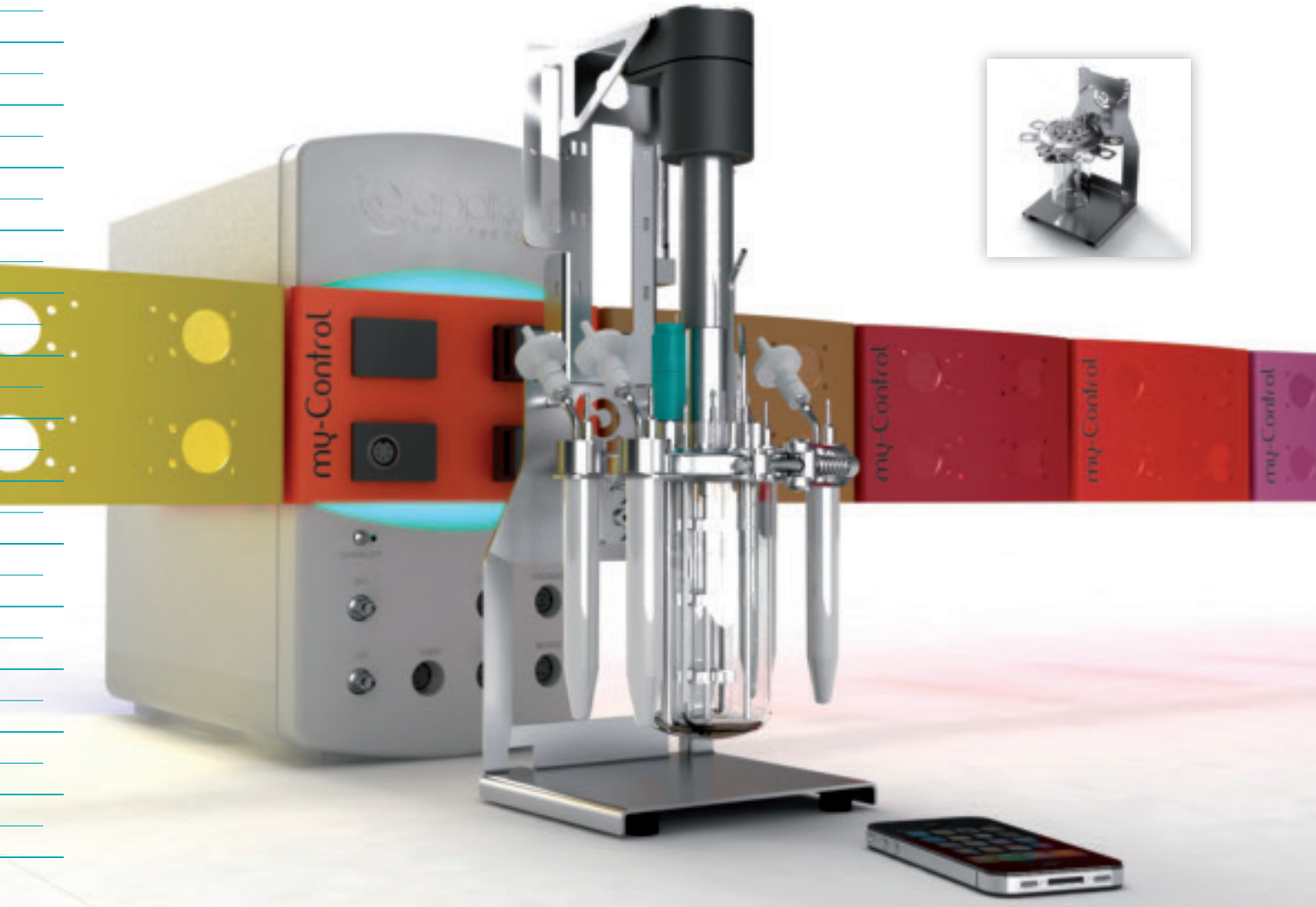
The MiniBio range of bioreactors (250 ml, 500 ml and 1000 ml total volume) is a true scale down of the laboratory scale bioreactor. The MiniBio systems have the same flexibility as the laboratory scale bioreactors. This means that the MiniBio systems can be customized to fit the demands of any process. The small volume reduces media costs and maximises bench space, which is normally at a premium.

Features

- Generate more data in less time
- Easy setup and operation
- Cultivate using less medium
- Cultivate using less bench space
- Generate scalable results

Applications

- Screening studies
- Media optimization
- Process optimization
- Microbial and Cell culture
  Batch, Fed-Batch, Perfusion and Continuous cultivation



Color your lab

Specifications

	MiniBio 250	MiniBio 500	MiniBio 1000
Total volume (ml)	290	550	1000
Working volume (ml)	200	400	800
Minimum working volume (ml)	50	100	200
Aspect ratio total volume	2.3	2.1	2.3
Aspect ratio working volume	1.6	1.5	1.9
Dimensions (dxh)	180 x 400 mm	195 x 400 mm	200 x 550 mm
Dimensions for autoclaving (dxh)	180 x 250 mm	195 x 250 mm	200 x 400 mm
Drive system	Direct drive, lipsealed	Direct drive, lipsealed	Direct drive, lipsealed
Maximum stirrer speed (rpm)	50 - 2000	50 - 1750	50 - 1500
Maximum impeller tip speed (m/s)	2.3	2.0	3.5
Impellers	Choice of Rushton and marine		
Gas sparger	Porous sparger or L-type sparger		
Gas overlay	Yes		
Exhaust gas	Electrically cooled exhaust gas condenser (evaporation <4% per day at 37°C @ 2vvm)		
Sampling	Fixed sample pipe with optional sampling system		
Draining	Height adjustable drain pipe		
Additions	4 fixed inlet ports and optional micro liquid injectors		
pH	Measurement: 8 mm classic pH sensor Control: via acid pump (variable speed pump) or CO_2 gas in combination with alkali pump (variable speed pump)		
DO_2	Measurement: 8 mm classic polarographic DO_2 sensor Control: via a combination of N_2, Air, O_2 (optional MFC) and agitation or nutrient addition (variable speed pump)		
Temperature	Measurement: Pt-100 sensor in thermowell in topplate Control: electrical cooling and heating jacket via bioreactor wall		
Foam	Measurement: Height adjustable conductivity based foam sensor Control: Anti foam addition (variable speed pump)		
Level	Measurement: Height adjustable conductivity based level sensor Control: variable speed pump for liquid addition or removal		
Optional inlets	Septum, chemostat tube, liquid entry system		
Optional sensors	Biomass, Optical Density, O_2 and CO_2 off gas.		

Glass autoclavable bioreactors, the world wide standard

In the laboratory bioreactor and fermentor range Applikon is worldwide market leader because of its dependable and easy to use systems. The bioreactors and fermentors excel in quality and modularity. An Applikon laboratory system is easy to upgrade if a change in research activities occurs. Applikon offers glass autoclavable bioreactors for cell culture applications and glass autoclavable fermentors for microbial culture applications. The systems are built according to the specific demands of a process using an extensive array of standard components. Because of the modularity and flexibility, the user can always adapt the systems to changed process demands. This results in low initial investment and low running costs. The stirred tank reactor (STR) is the most widely used bioreactor type. Glass autoclavable bioreactors and fermentors are available in 1 - 2 - 3 - 5 - 7 - 15 and 20 liter total volume.

Features

- Wide range of volumes with interchangeable modules
- Wide range of modules to tailor the systems to the research demands
- No welded parts in the bioreactor topplate
- Simple set-up and easy to handle
- Optional high torque magnetically coupled agitator
- All metal parts are constructed of stainless steel 316L
- External mirror polished finish
- Electropolished finish of product contact stainless steel parts ease cleanability
- Glass dished bottom vessels are made of borosilicate glass to guarantee:
  - resistance to thermal shock
  - excellent corrosion resistance
  - smooth, non porous surface for easy cleaning
  - optimal transparency for visual inspection of the culture
- Glass bioreactor vessels can be used up to 0.5 barg (7.5 psig) of overpressure.

Applications

- Microbial cultures
- Cell cultures
- Batch
- Fed-Batch
- Perfusion
- Continuous cultivation

Specifications

	Total volume (L)	Working volume (L)	Minimum working volume (L)	Aspect ratio total volume (L)	Aspect ratio working volume (L)
1 liter	1.25	0.9	0.3	2.1	1.5
2 liter single wall	2.2	1.7	0.5	2.2	1.9
2 liter jacketed	2.2	1.7	0.5	2.2	1.9
3 liter single wall	3.1	2.7	0.5	1.9	1.5
3 liter jacketed	3.1	2.7	0.5	1.9	1.5
5 liter single wall	4.8	3.4	0.9	1.6	1.1
5 liter jacketed	4.8	3.4	0.9	1.6	1.1
7 liter single wall	6.8	5.4	1.5	2.2	1.8
7 liter jacketed	6.8	5.4	1.5	2.2	1.8
15 liter single wall	16.5	12	3.0	1.7	1.5
15 liter jacketed	18.2	12	3.0	1.5	1.2
20 liter single wall	23.4	16	3.0	2.4	2.0

	Internal Diameter (mm)	Internal Height (mm)	Autoclave dimensions (WxH mm)
1 liter	95	200	ø172 x 393
2 liter single wall	105	240	ø190 x 436
2 liter jacketed	105	240	ø219 x 486
3 liter single wall	130	240	ø190 x 436
3 liter jacketed	130	240	ø235 x 436
5 liter single wall	160	250	ø260 x 436
5 liter jacketed	160	250	ø260 x 480
7 liter single wall	160	350	ø260 x 600
7 liter jacketed	160	350	ø264 x 645
15 liter single wall	222	440	ø381 x 710
15 liter jacketed	240	440	ø391 x 740
20 liter single wall	222	620	ø381 x 900

Drive system	Direct drive, lipsealed or magnetically coupled
Maximum stirrer speed (rpm)	Standard range is 50 - 1250. 1, 2 and 3 liter systems can be supplied with 2000 rpm motor
Impellers	Rushton and marine with outside diameters 45 mm, 60 mm 75 mm or 85 mm
Gas sparger	Porous sparger or L-type sparger
Gas overlay	Yes
Exhaust gas	Water cooled exhaust gas condenser
Sampling	Fixed height or height adjustable sample pipe with optional sampling system Sample pipe internal diameters choices are: 1.7 mm, 4 mm, 6 mm or 10 mm
Draining	Drain pipe
Additions	Triple or single inlet ports and optional micro liquid injectors
pH	Measurement: 12 mm classic pH sensor
	Control: via acid pump or CO_2 gas (rotameter or MFC) in combination with alkali pump
DO_2	Measurement: 12 mm classic polarographic DO_2 sensor Control: via a combination of N_2, Air, O_2 (Rotameter or MFC) and agitation or nutrient addition pump
Temperature	Measurement: Pt-100 sensor in thermowell in topplate Control: cooling and/or heating jacket via bioreactor wall or via internal heat exchanger
Foam	Measurement: Height adjustable conductivity based foam sensor Control: Anti foam addition pump
Level	Measurement: Height adjustable conductivity based level sensor Control: pump for liquid addition or removal
Optional inlets	Septum, chemostat tube, liquid entry system

Photo bioreactors, the next best thing to sunlight

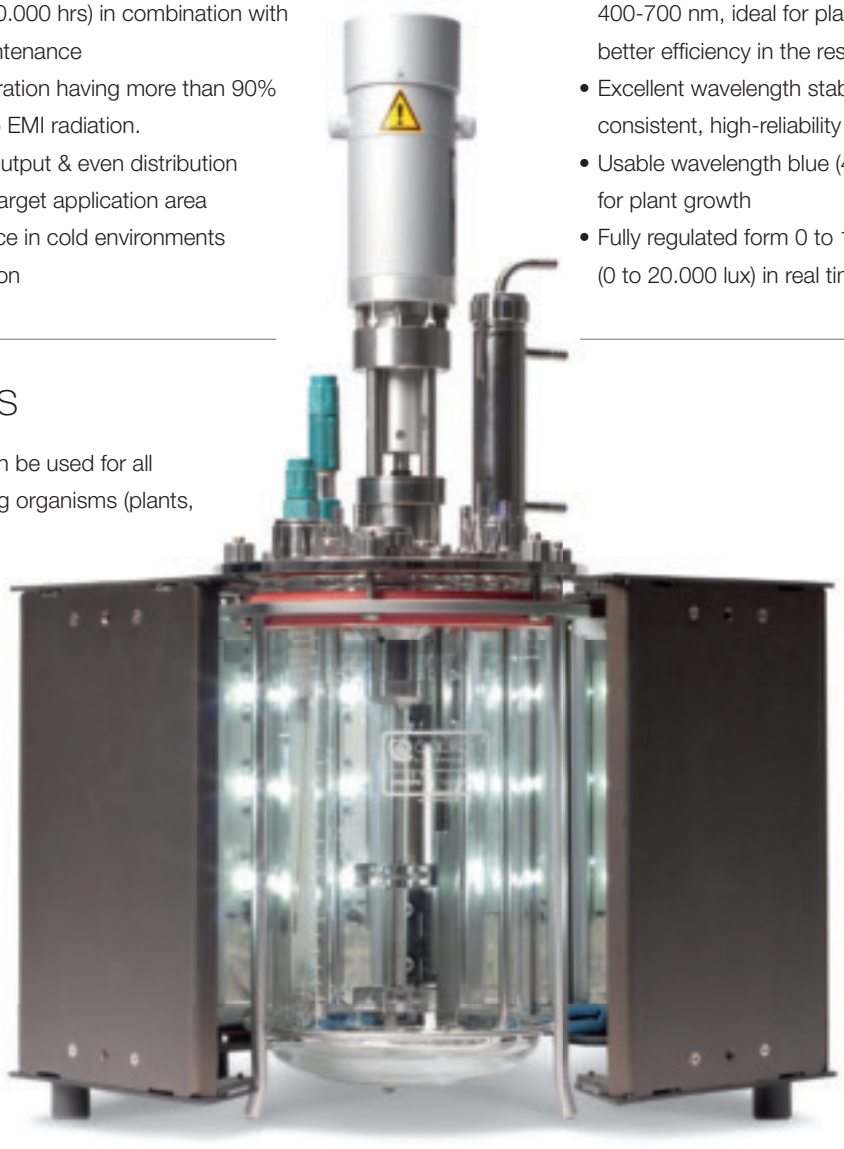
The Applikon “PhotoBio” photobioreactor range is based on the standard Applikon re-usable and single-use bioreactors. Special light panels are added to these systems to allow the growth of photosynthesizing organisms (plants, algae, bacteria).
The well proven design of the bioreactors in combination with the state-of-the-art LED light panels guarantee the best performance of the PhotoBio for any application. The light panels can be retrofitted to the Applikon bioreactors to turn your standard bioreactor into a photobioreactor with no downtime and minimal investment.

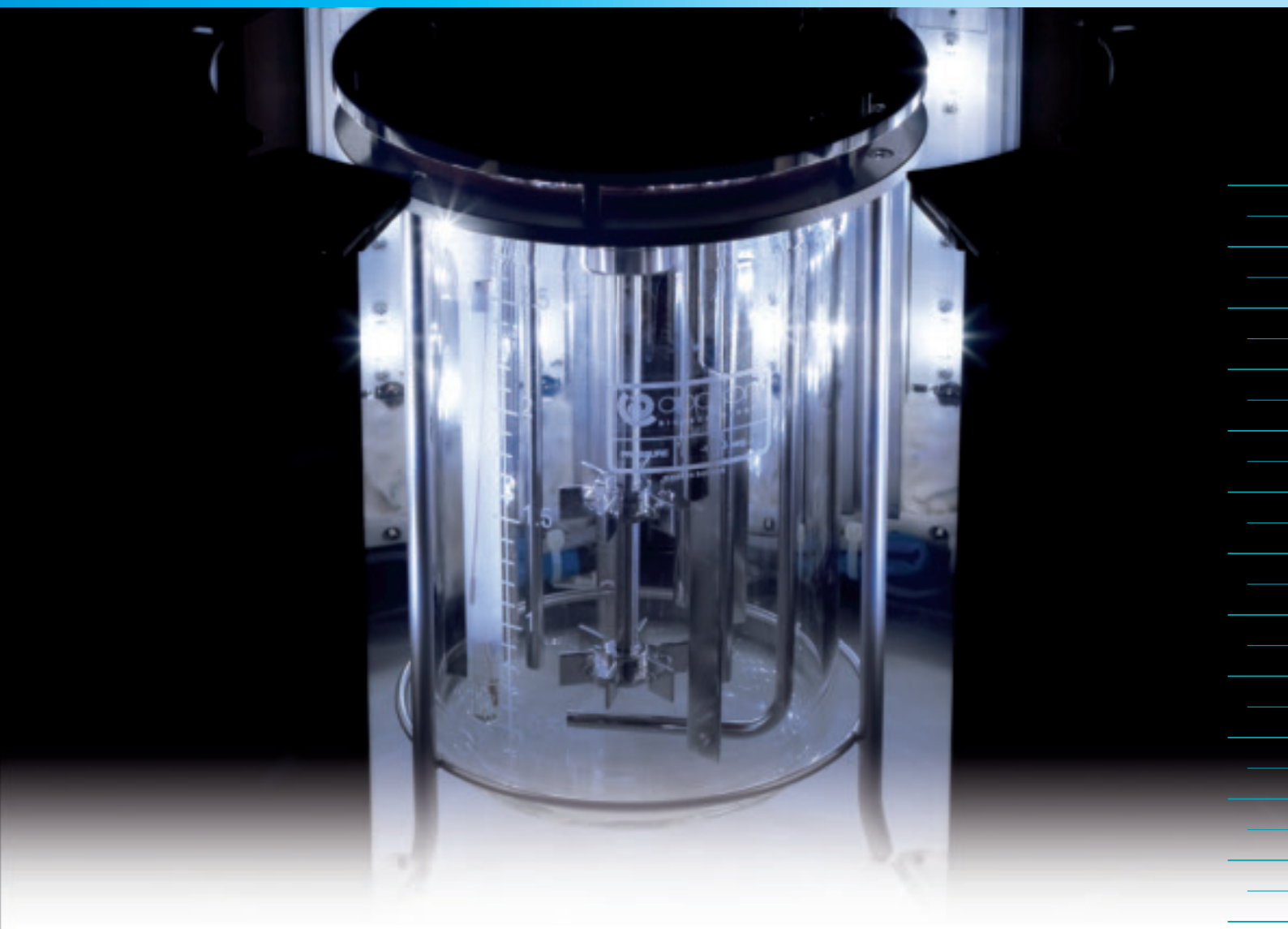
Features

- Proven bioreactor design
- Long lifetime (100.000 hrs) in combination with good lumen maintenance
- Low voltage operation having more than 90% efficiency with no EMI radiation.
- Directional light output & even distribution of light over the target application area
- Great performance in cold environments
- No heat generation
- Photo-synthetically Active Radiation (PAR) 400-700 nm, ideal for plant growth, to achieve better efficiency in the response of plants
- Excellent wavelength stability over time, consistent, high-reliability
- Usable wavelength blue (470 nm) and red (660 nm) for plant growth
- Fully regulated form 0 to 100% light intensities (0 to 20.000 lux) in real time

Applications

- The PhotoBio can be used for all photosynthesizing organisms (plants, algae, bacteria).





Specifications

Maximum driving capacity	140 watt of power or 24 light bank of 6 watt
Programmable zones	8
Intensity control	0 to 100% PWM
Time base	Built in Real time clock
Time range	99:59 hours: minutes per step (maximum 9 time/intensity steps in one cycle)
Light driving	Constant current source
Housing & Protection Class	IP-30 and IP-65 for Control Panel and IP67 for Light bank
User interface	16 x 2 Backlit LCD, Feather touch keys
Serial Communication port	Full duplex RS232 or RS485 interface(optional)
Ambient temperature	0 °C up to 60 °C
Power supply	115 / 230 V AC, 50-60 Hz
Power consumption	Maximum 150 W

The PhotoBio range of bioreactors consist of the following products:		
PhotoBioSTR2	2 liter stirred tank bioreactors (single wall, non jacketed),	40 Watt panel
PhotoBioSTR3	3 liter stirred tank bioreactors (single wall, non jacketed)	40 Watt panel
PhotoBioSTR5	5 liter stirred tank bioreactors (single wall, non jacketed)	60 Watt panel
PhotoBioSTR7	7 liter stirred tank bioreactors (single wall, non jacketed)	60 Watt panel
PhotoBioSTR15	15 liter stirred tank bioreactors (single wall, non jacketed)	120 Watt panel
PhotoBioSTR20	20 liter stirred tank bioreactors (single wall, non jacketed)	120 Watt panel
PhotoBioSU10	10 liter single use AppliFlex rocking bioreactors	40 Watt panel
PhotoBioSU20	20 liter single use AppliFlex rocking bioreactors	60 Watt panel
PhotoBioSU50	50 liter single use AppliFlex rocking bioreactors	120 Watt panel

Single use bioreactors

Applikon offers several types of single-use bioreactors: AppliFlex, rocking bioreactors from 10 to 50 liter, HyClone SUB stirred tank bioreactors in the range of 66 to 2,700 liter total volume, ATMI PAD square bioreactors in the range of 25 to 2,500 liter total volume and ATMI iCellis Nano bioreactors for cultivating anchorage dependable cells. All systems are unique in their accurate measurement and control of key process parameters.

The systems can be controlled using the Applikon ez-Control, i-Control or my-Control. Most systems can be equipped with re-usable sensors as well as fluorophor pH and Dissolved Oxygen sensors. All systems are supplied turnkey and fully documented. All systems go through standard IQ/OQ and FAT procedures before they are delivered and installed at the customers site. The qualified Applikon technical support team can take care of the installation and will be your first point of contact for any questions. Our delivery includes the bioreactor, the controller, sensors, actuators, temperature control system, supervisory software and validation documentation. Our well trained sales consultants are able to advise you on the complete configuration of your single use bioreactor system.

AppliFlex

The AppliFlex bioreactor range consists of a 10 liter, 20 liter and 50 liter bioreactor bag. The control system (pH, Dissolved Oxygen, temperature, mixing) is the standard Applikon ez-Control. The rocking motion offers gentle mixing. The same rocker can be used for the 10 (2x), 20 and 50 Liter bioreactor bags. The AppliFlex bioreactors are an easy scale-up to the HyClone bioreactors; the bags are made of the same materials which eases validation.

HyClone® S.U.B.

The HyClone® S.U.B. provides all the advantages of single-use bioprocessing in a classical stirred tank bioreactor system design. The critical design parameters of the S.U.B., such as height to diameter ratios, mixer design and location and typical control system interfaces, have been maintained. The S.U.B. is available with new optimized standard BioProcess Containers with improved dual sparge capability. Open pipe and frit sparging systems are included to provide a wider range of operating conditions. A key element to the single-use design is the plastic (polyethylene) impeller with a bearing/seal assembly linked to an external mixer drive. The range includes units with maximum working volumes of 50, 100, 250, 500, 1,000 and 2,000 L.

ATMI iCELLis™ Nano

The ATMI iCELLis™ Nano system, is designed to simplify your process by combining the advantages of single-use technologies with the benefits of a fixed-bed system. Central to the iCELLis bioreactor technology is the use of a compact fixed-bed, filled with macrocarriers. This matrix is made of medical grade polyester microfibers and provides up to 4 m^2 available area for cell growth in only 200 ml volume.
This is the surface-equivalent of 47 roller bottles. The iCELLis bioreactor is provided with pre-packed macrocarriers. Evenly-distributed media circulation is achieved by a built-in magnetic drive impeller, ensuring low shear stress and high cell viability. The cell culture medium flows through the fixed-bed from the bottom to the top. At the top, the medium falls down the outer wall as a thin film where it takes up O_2 to maintain high k_La the in the bioreactor.

- iCELLis nano Fixed-bed height 10 cm
- Fixed-Bed Volume 0.2 L
- Culture Surface Area 4 m^2
- Equivalent CS10 (6,300 cm^2) 6
- Equivalent RB (850 cm^2) 47

ATMI PadReactor

The ATMI PadReactor system is perfectly suited to laboratory environments, process development centers, clinical material supply and flexible GMP manufacturing. The square bioreactor vessel, which offers comparable functionality to classical stirred tank bioreactors, is a single-use bag integrating an internal paddle mixing and sparger system. The sparger is integrated in the paddle mixer to enhance oxygen transfer rates.
The innovative bag design improves mixing at low shear forces and allows a non-invasive stirrer connection to the system. The paddle is enclosed in a medical grade ULDPE sleeve, made from the same contact material as the bag itself, and is coupled on top of the vessel with the mechanical mixing head. The PadReactor is available in total volumes of 25L, 50L, 250L, 600L, 1200L and has been used successfully in cultivation of anchorage dependent and suspension cells.

Specifications

	AppliFlex	10	25	50				
	Total volume (L)	10	25	50				
	Max working volume (L)	5	12.5	25				
	Min working volume (L)	2	5	10				
	Hyclone	50	100	250	500	1000	2000	
	Total volume (L)	66	120	316	660	1320	2700	
	Max working volume (L)	50	100	250	500	1000	2000	
	Min working volume (L)	25	50	125	250	500	1000	
	Pad	Mini	25	50	125	250	600	1200
	Total volume (L)	16	25	50	125	250	600	1200
	Max working volume (L)	13	20	40	100	200	480	960
	Min working volume (L)	3.2	8	10	25	25	120	240
	iCellis Nano							
	Volume (L)	0.04	0.08	0.2				
	Surface area Low (m^2)	0.53	1.06	2.6				
	Surface area High (m^2)	0.8	1.6	4				

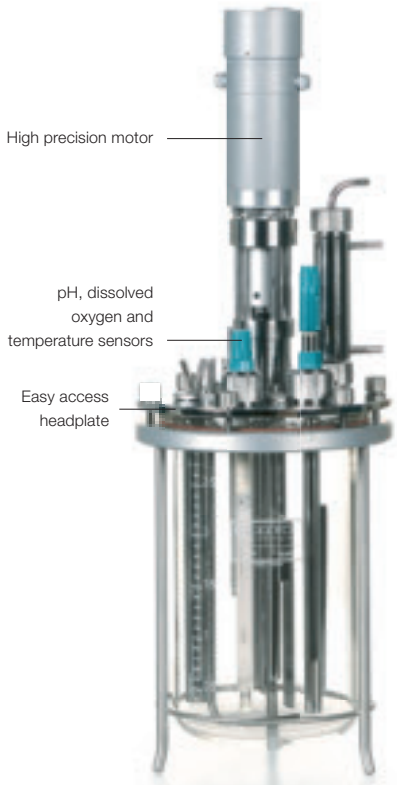
Sensors	**Fluorophor pH**	**Fluorophor Dissolved Oxygen**	**Gel filled sterilizable pH**	**Sterilizable Polarographic Dissolved Oxygen**	**Temperature**
Measuring range	5.5 ... 8.5 pH	0 ... 100% O_2 saturation	0 ... 12 pH	0 ... 100% O_2 saturation	0 ... 150°C
Accuracy	± 0.1 pH	± 0.4%	± 0.1 pH	± 2%	0.1°C
Measuring temperature range	0 - 40°C	0 - 40°C	0 - 80°C	0 - 60°C	0 .. 150°C
Maximum temperature	45°C	45°C	135°C	135°C	150°C
Sensor life time	2 weeks @ 1 measurement per minute	6 months	> 1 year	> 1 year	> 1 year
	3.5 weeks @ 1 measurement per 2 minutes				

Features & Applications

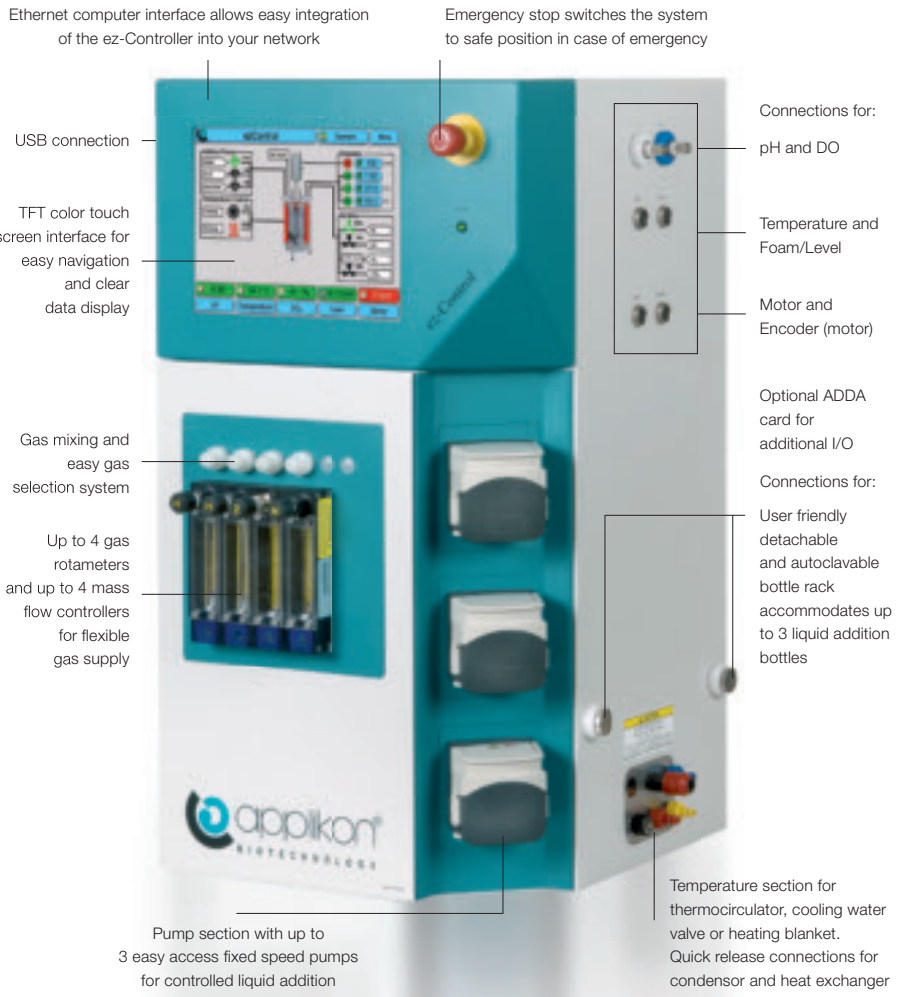
- Simple operation
- OPC compliant controller
- Accurate process control
- Classic and single-use (fluorophor) sensors for measurement of pH, Dissolved Oxygen
- Accurate control of pH, DO, temperature, mixing
- Data logging & SCADA (21CFR part 11) available
- Turn-key delivery
- IQ/OQ/FAT and SAT for the complete system
- Fully documented delivery eases validation
- One point of contact for the complete system
- Qualified support and service
- Cell culture
- Batch
- Fed Batch
- Perfusion
- Suspension cells
- Anchorage dependent cells

BioBundle, complete cultivation systems

A BioBundle is a complete bioreactor system, equipped with all necessary components and is ready to use “out-of-the-box”. No detail is overlooked: the system is complete with silicone tubing, sample bottles and a “starter kit” including spare parts. The BioBundle is easy to set-up, requires no special skills or tools, easy to learn and easy to operate. BioXpert Lite Software for data acquisition is included. Select one or more of the optional add-on packs to customize your BioBundle. The BioBundle provides a unique

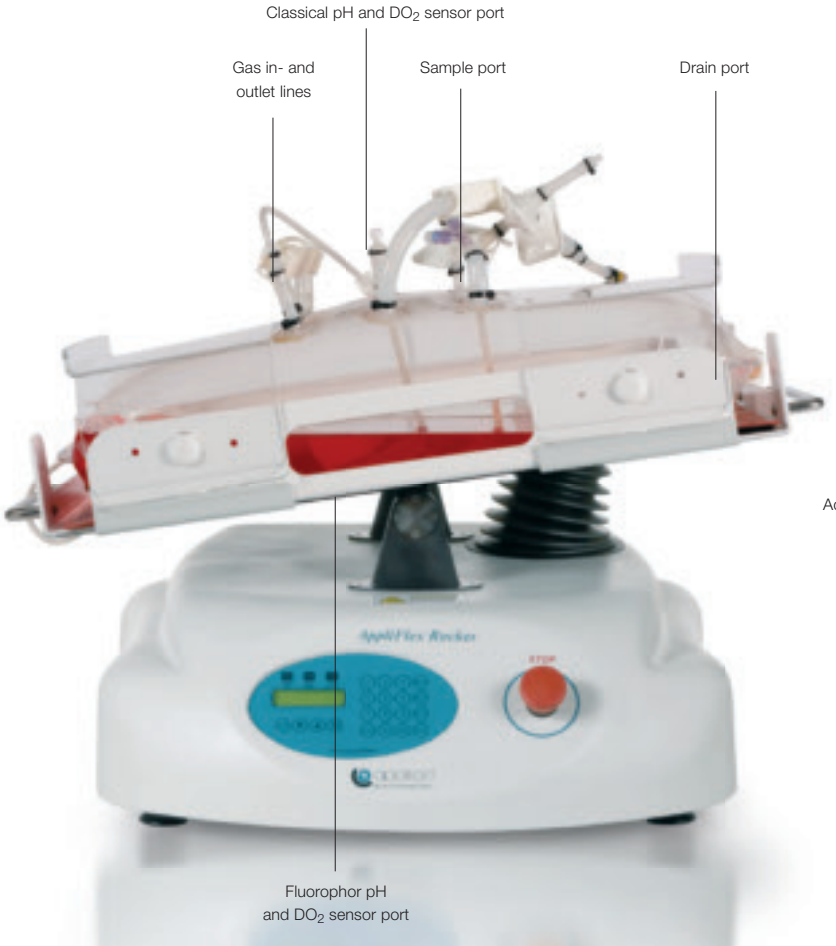


Autoclavable glass bioreactor

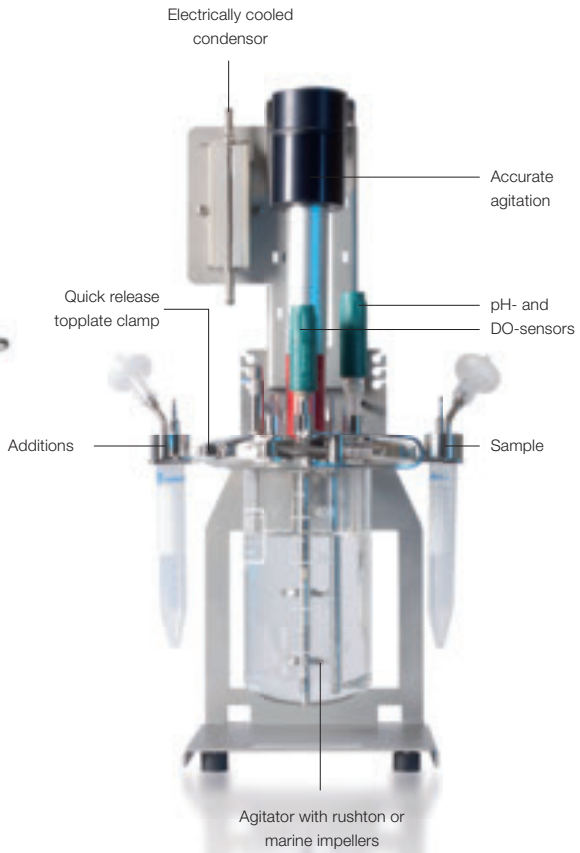

Ethernet computer interface allows easy integration of the ez-Controller into your network
Emergency stop switches the system to safe position in case of emergency
USB connection
TFT color touch screen interface for easy navigation and clear data display
Gas mixing and easy gas selection system
Up to 4 gas rotameters and up to 4 mass flow controllers for flexible gas supply
Pump section with up to 3 easy access fixed speed pumps for controlled liquid addition
Connections for:
pH and DO
Temperature and Foam/Level
Motor and Encoder (motor)
Optional ADDA card for additional I/O
Connections for:
User friendly detachable and autoclavable bottle rack accommodates up to 3 liquid addition bottles
Temperature section for thermocirculator, cooling water valve or heating blanket. Quick release connections for condensor and heat exchanger

ez-Control

combination of ease of use and sophistication, reducing the time to start-up a process. The system is equipped with the intelligent and powerful process controller: easy and intuitive to operate, such that the user manual might not be needed.
The process controller has control loops for pH, Temperature, Dissolved Oxygen, Foam/Level and agitation and can apply a combination of digital and analog outputs for process control. Actuators such as rotameters, solenoid valves, mass flow controllers, pumps, thermocirculator and others can be controlled. The operator can set P-I-D values, dead-band for pH control, cascade control strategies, and dose monitors for liquid additions. The advanced auto-tuning adaptive control system is part of every bundle and takes the guessing out of PID controller setting. The system can automatically and continuously calculate the best controller settings for every process.



AppliFlex



MiniBio

Modularity and configurability

Although the BioBundle has a pre-set configuration, the whole bioreactor system remains modular and configurable. With simple changes in configuration the BioBundle system can be modified for different applications in a cost-effective way! This applies to changes in process control strategies, in using extra gas or liquids, but also in changing the system into a microbial or cell culture set-up.

Compact design

The BioBundle is designed to occupy as small a footprint as possible. All accessories such as pumps and gas flow control valves are conveniently integrated in a compact console. The compact design reduces the need for expensive lab space.

Software for data acquisition and supervisory control

The BioBundle control system includes an Ethernet connection port to connect to a PC with software for data acquisition or SCADA such as the Applikon BioXpert packages.
BioXpert Lite (data acquisition) is included in this BioBundle. Multiple bioreactors can be connected to one PC for data acquisition.
Optional BioXpert packages are BioXpert 2 and BioXpert W7: SCADA of multiple bioreactors, including cGMP production applications.

Cost Saving

The BioBundle is a pre-packed system. The assembling of the BioBundles in series provides a cost saving which is for the benefit of the customer.

Summarising

Over all some of the benefits Applikon bioreactors provide include:

- dependable and reliable operation = greater productivity and yield
- modular design = less cost in the future (being able to use same equipment for different applications)
- less downtime due to maintenance = greater economy in operation, higher yield to cost ratio
- simple operation = less operator training required

Specifications

	MiniBioBundle Cell Culture	MiniBioBundle Microbial	BioBundle Cell Culture	BioBundle Microbial	AppliFlex BioBundle
Control system	my-Control	my-Control	ez-Control	ez-Control	ez-Control
Total Volume	250ml, 500 ml, 1000ml	250ml, 500 ml, 1000ml	1L, 2L, 3L, 5L, 7L, 15L, 20L	1L, 2L, 3L, 5L, 7L, 15L, 20L	10L, 20L, 50L
Working Volume	200ml, 400ml, 800ml	200ml, 400ml, 800ml	0.9L, 1.7L, 2.7L, 3.2L, 5.4L, 12L, 16L	0.9L, 1.7L, 2.7L, 3.2L, 5.4L, 12L, 16L	5L, 10L, 25L
Agitator	Lipseal with marine impeller	Lipseal with Rushton impellers	Lipseal with marine impeller	Lipseal with Rushton impellers	Mixing by rocking motion
Aeration	Air supply via sparger	Air supply via sparger	Air and Oxygen supply via sparger	Air and Oxygen supply via sparger and overlay	Air and Oxygen supply via overlay
Exhaust gas	Optional gas outlet condenser	Gas outlet condenser	Gas outlet condenser	Gas outlet condenser	
Sampling	Sample pipe included	Sample pipe included	Sample pipe included	Sample pipe included	Sample line included
	Sample system optional	Sample system optional	Sample system optional	Sample system optional	Sample system optional
pH	Measurement via pH sensor control via liquid alkali pump and CO_2 gas supply	Measurement via pH sensor control via liquid alkali or acid addition pump	Measurement via pH sensor control via liquid alkali pump and CO_2 gas supply	Measurement via pH sensor control via liquid alkali and acid addition pump	Measurement via pH sensor control via liquid alkali pump and CO_2 gas supply
Temperature	Measurement via Pt-100	Measurement via Pt-100	Measurement via Pt-100	Measurement via Pt-100	Measurement via Pt-100
	Heating only via heating blanket	Heating and cooling via Peltier system	Heating only via heating blanket	Heating via heating blanket cooling by cold water in heat exchanger	Heating only via heating blanket
Dissolved Oxygen	Measurement via DO_2 sensor control via Air and O_2 gas supply	Measurement via DO_2 sensor control via Air supply and agitation speed	Measurement via DO_2 sensor control via Air and O_2 gas supply	Measurement via DO_2 sensor control via Air and O_2 supply and agitation speed	Measurement via DO_2 sensor control via Air and O_2 gas supply
Foam	Option	Measurement via Foam sensor control via anti-foam addition pump	Option	Measurement via Foam sensor control via anti-foam addition pump	
Level	Option	Option	Option	Option	
Liquid additions	4 fixed in topplate and 1 septum port	4 fixed in topplate and 1 septum port	3 ports in triple inlet and one inoculum port.	3 ports in triple inlet, one inoculum port 1 and septum port.	One inoculum and alkali inlet.
	One liquid storage system included	Two liquid storage systems included	One liquid storage system included	Three liquid storage systems included	One liquid storage system included
Start-up kit	Included	Included	Included	Included	Included
BioXpert Lite software	Included	Included	Included	Included	Included

my-Control, color your lab

my-Control is the most advanced bioreactor controller for small scale bioreactors starting at 50 ml (working volume). The system can control bioreactors up to a total volume of 3 L. This versatile controller can be used for both cell culture and microbial cultures.
The advanced software makes it possible to switch from microbial to cell culture configuration in seconds. With its footprint of only 19 by 35 cm (W x D) it uses the minimal amount of bench space, allowing to set up as many as 5 on 1 m width of bench space.
The built-in web server allows the my-Control to be operated by any computer with a web browser (Internet Explorer, Mozilla Firefox, Apple Safari or Google Chrome). Wireless devices like iPad, iPhone or Android tablets or phones can also be used to operate my-Control. The selectable colored band on the unit allows the system to be personalized and to fit your laboratory.

Features

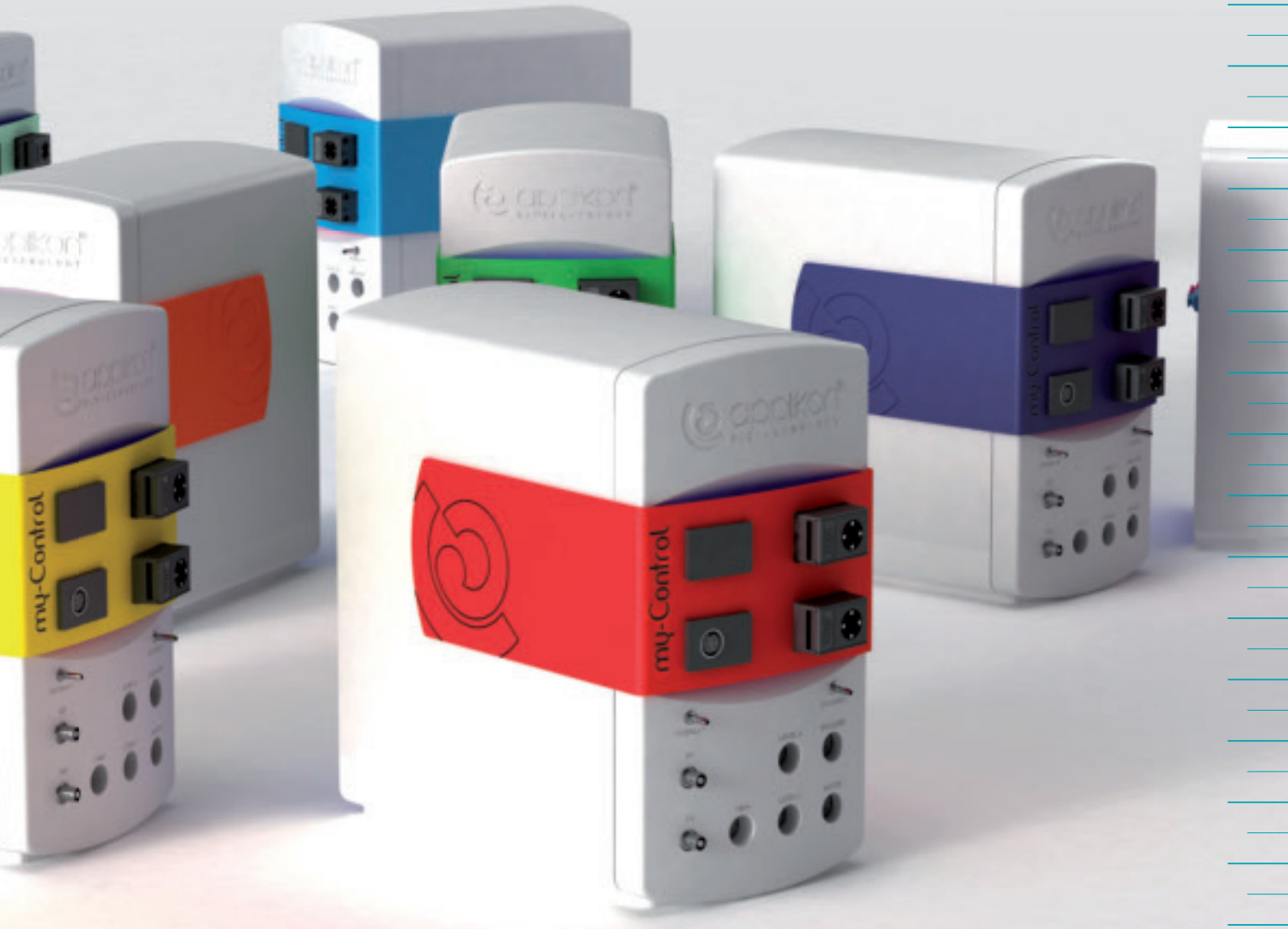
- Control of all bioprocess parameters (including pH, temperature, dissolved oxygen, agitation, foam and level)
- Selectable autotuning adaptive PID control for accurate control when process conditions change during the culture.
- Easy operation through web browsers (Windows PC, Apple PC, Linux PC, iPhone, iPad, Android tablet, Android phone)
- Parallel processing is enhanced by allowing up to 32 my-Controllers in one human interface
- Extended liquid additions options tuned to small scale cultivation via up to 6 digital variable speed pumps or micro addition valves for extremely accurate nanoliter volumes
- Enhanced gas addition strategies via 3 mass flow controllers
- No water connections needed due to electrical cooling and heating system for bioreactor and condenser
- Expandable control system with optional extra inputs and outputs
- USB connection for optional balances, Biomass or Fluorophor pH and DO sensors

Applications

- Ideal for screening, media optimisation, modelling, toxicity studies etc.
- Mini bioreactors
- Autoclavable bioreactors up to 3 liter volume
- Single Use Bioreactors up to 3 liter volume
- Microbial and Cell cultivation
- Batch, Fed-Batch, Perfusion and Continuous cultivation

Specifications

Inputs	pH, temperature, dissolved oxygen, agitation, foam and level
	Optional: biomass and fluorophor pH and fluorophor dissolved oxygen
	Optional inputs 4 x analog in (0 - 10 V)
Control type	PID control with selectable autotuning adaptive control
Actuators	Up to 6 digital variable speed pumps or micro addition valves for addition of extremely accurate nanoliter volumes
	Up to 3 Mass Flow Controllers or 4 solenoid valves for gas flow control
	Electrical bioreactor heating via Peltier element or Heating Blanket
	Electrical bioreactor cooling via Peltier element
	Electrical condenser cooling via Peltier element
	Spare I/O: 8 x digital output, 4 x analog out (0/4 - 20 mA)
Additional features	Emergency stop connection, central alarm output,
	System status indication (inactive/active/alarm) by integrated colored light
Power	Pmax = 480 VA, 115 / 230 Vac
Dimensions (d x w x h)	350 x 190 x 400 mm (D x W x H)
Weight (kg)	8.5 kg



in-Control, simply powerful

in-Control is a process controller for laboratory scale bioreactors. The system is a drop-in-replacement for our older ADI 1010 Bio Controller and ADI 1030 Bio Controller. The in-Control offers high level control on a small footprint. When you are running your bioreactors controlled by our ADI 1010 or ADI 1030 Bio Controllers, the in-Control can be used to increase the capabilities of your bioreactor system with a minimal investment and no downtime for your process. The controller can be used for both cell culture and microbial cultures. The intuitive human interface is a built-in color touch screen.

Features

- Control of all bioprocess parameters (including pH, temperature, dissolved oxygen, agitation, foam and level)
- Selectable autotuning adaptive PID control for accurate control when process conditions change during the culture.
- Easy operation through touch screen interface and through web browsers (Windows PC ,Apple PC, Linux PC, iPhone, iPad, Android tablet, Android phone)
- Enhanced gas addition strategies via up to 4 Mass Flow Controllers
- Expandable control system with optional extra inputs and outputs
- USB connection for optional biomass or fluorophor pH and DO sensors and balances
- Ethernet communication to SCADA

Applications

- Replacement of ADI 1010 Bio Controller and ADI 1030 Bio Controller
- Autoclavable bioreactors up to 20 liter volume
- Single Use Bioreactors
- Microbial and Cell cultivation
- Batch, Fed-Batch, Perfusion and Continuous cultivation

Specifications

Inputs	pH, temperature, dissolved oxygen, agitation, foam and level
	Optional: biomass and fluorophor pH and fluorophor dissolved oxygen
	Optional inputs 4 x analog in (0 – 10 V)
Control type	PID control with selectable autotuning adaptive control
Actuators	8 x digital outputs for heating, cooling, fixed speed pump, solenoid valves etc.
	Up to 4 Mass Flow Controllers or 4 solenoid valves for gas flow control
	Spare I/O: 4 x analog out (0/4 – 20 mA)
Additional features	Emergency stop connection, central alarm output,
Power	Pmax: 480 VA 230 / 115 Vac
Dimensions (dxwxh)	322 x 312 x 210 mm
Weight (kg)	7.2 kg

ez-Control, total control at your fingertips

The ez-Control accurately controls pH, Temperature, Dissolved Oxygen, Foam/Level and Agitation in bioreactors and fermentors. The color touch screen interface guides the user through the intuitive operation. The adaptive control features allow the user to focus on the process while the controller keeps tight control on the important process parameters. What makes this controller unique are its ease of use, its small footprint, its flexibility and its accurate control. The optional ADDA board offers an additional 8 analog inputs, 4 analog outputs, 8 digital inputs and 8 digital outputs.

Features

- Simple operation
- Adaptive PID control
- OPC compliance
- User definable controlloop configuration
- Store, copy and reload process configurations
- Local data storage and display up to 72 hours
- Synoptic, trending and bar graph displays
- Multiple user levels

Applications

- Autoclavable bioreactors
- Steam in Place bioreactors
- Single Use Bioreactors
- Microbial and Cell cultivation
- Batch, Fed-Batch, Perfusion and Continuous cultivation

Specifications

	Measurement range	Measurement accuracy
pH	0 - 14 pH	0.01 pH
Temperature	0 - 150 °C	0.1°C
Dissolved Oxygen	0 - 100% saturation	0.1%
Foam/Level	Conductivity based measurement	On / off control
Agitation	0 - 1250 rpm	1 rpm
	0 - 2000 rpm	1 rpm
Analog in	8 x	
Analog out	4 x	
Digital in	8 x	
Digital out	8 x	
Fluorophor pH	Optional 5.5 - 8.5 pH	± 0.1 pH
Fluorophor Dissolved Oxygen	Optional 0 - 100% saturation	± 0.1 %
Biomass	Optional	
Display	10.4 Inch color display with resistive touchscreen	
Communication interfaces	1 x Ethernet port (computer communication)	
	2 x USB slave,	
	1 x USB master	
Control type	PID control with selectable auto-tuning adaptive control	
Actuators	Up to 3 fixed speed pumps	
	Up to 4 Mass Flow Controllers	
	Heating and cooling via thermocirculator, heating blanket, cooling water valve	
	Water cooled condenser connection	
Additional features	Emergency stop connection, central alarm output,	
	Color touch screen operation	
Process connections	2 x Gas outlet, water for condenser (in and out),	
	Water for temperature control (in and out)	
Power	230 Vac 50 Hb / 115 Vac 60 Hb	
Dimensions (dxwxh)	474 x 408 x 711 mm	
Weight (kg)	30 kg	

i-Control, the scalable control system

i-Control is an easy to operate bioreactor control system and utility console. This scalable control solution is used to control processes in bioreactor systems from laboratory scale to pilot plant and production scale saving time and money during scale-up. The i-Control is available in a Single, a Dual bioreactor set-up as well as in a Quad (4 bioreactors) configuration. This standard control solution can be supplied with Allen Bradley or Siemens PLC's. Basic functionality includes advanced process control for numerous parameters, fully automatic sterilization and Clean In Place routines. The off-the shelf system is supplied pre-configured and ready to use.

Features

- Off-the shelf standard Solution
- Reliable control platform (Allen Bradley and Siemens hard- and software)
- Supplier independent solution based on industry standard hardware
- Local Control and local display
- Integrates with any factory automation system
- Cost effective
- Fully documented supply eases validation
- Can be used in a 21CFR part 11 compliant system

Applications

- Laboratory scale bioreactors
- Pilot plant scale bioreactors
- Production scale bioreactors
- Microbial cultures
- Cell cultures

Specifications

pH/Temp input		
pH amplifier	Range	0 pH 14 pH
	Accuracy	± 0.01 pH
Temperature amplifier	Type	Pt 100 (3-wire type)
	Range	0°C +150°C
	Accuracy	± 0.1°C
DO/Level input		
DO amplifier	Type	Polarographic
	Range	0 % 500 % (air)
	Accuracy	± 0.1 %
Level amplifier	Type	On/Off signal
	Sensitivity	Software-selectable:
	High	Conductivity ≥ 26 µS equals “Contact”
	Low	Conductivity ≥ 200 µS equals “Contact”
2 Channel analog inputs	Range	4 – 20 mA
	Accuracy	± 0.1% Full Scale value
2 Channel analog outputs	Range	4 – 20 mA
	Accuracy	± 0.1% Full Scale value
2 Channel analog inputs for RTDs	Sensor Type	Pt-100
	Range	-200°C . . .+800°C
	Accuracy	± 0.2 % Full Scale value
	Resolution	0.1°C

BioXpert®, supervisory control and data aquisition

BioXpert is a software tool to control bio-processes and to store the process data. The software is designed specifically for biotech researchers and operators in the bio-environment. The logical structure of the program and the user-friendly interface allows the program to be used by anyone. That is why over 3,000 copies of our BioXpert software are in use worldwide. The software is easy to operate and has extensive functionality for monitoring, collecting and storing data and controlling processes

Various BioXpert versions have been developed based on international standards for use in either research and pilot plant or production environments. BioXpert Lite is designed for data collection, data storage and data presentation. The research version (BioXpert 2) offers maximum flexibility to set up and to modify processes. The pilot plant and production version (BioXpert W7) focuses on process repeatability and data security.

Features

BioXpert seamlessly integrates with Applikon and other makes of controllers and peripheral equipment to enable you to get the maximum out of your cultivation system. Pre-defined recipes exist for microbial culture, mammalian cell culture and plant cell culture. All process data and controller data can be stored at user-defined intervals. Off-line measurements can be added to the process data to be used for calculations or advanced process control. BioXpert offers different ways of presenting your measured data: trend graph, table and bar graph. The on-line calculations of BioXpert can be used to calculate derived variables. The statement editor and interpreter allow time and/or event based execution of advanced control strategies. Another option for supervisory control is the use of timed profiles. Remote Access for BioXpert W7 makes process data accessible for monitoring throughout a network using web browser technology.

Applications

- BioXpert software can be used for Microbial and Cell cultures in Batch, Fed-Batch, Perfusion and Continuous cultivation

Specifications

Specifications	**BioXpert Lite**	**BioXpert 2**	**BioXpert W7**
General			
Operating system	Windows NT, 2000, XP, Vista, Windows 7 (32 bit)	Windows NT, 2000, XP, Vista, Windows 7 (32 bit)	Windows XP (service pack 3) Vista Windows 7 (32 bit)
Communication drivers include	ADI 1010, ADI 1020, ADI 1030,	ADI 1010, ADI 1020, ADI 1030, ADI 1060	ADI 1010, ADI 1030, ADI 1060
	my-Control	my-Control	my-Control (via OPC)
	ez-Control	ez-Control	ez-Control (via OPC)
	in-Control	in-Control	in-Control (via OPC)
			i-Control (via OPC)
	AppliFlex Rocker	AppliFlex Rocker	AppliFlex Rocker
	Balances	Balances	
Additional drivers available separately	no	no	yes
	ADDA card	ADDA card	
Measurement of process values from process controllers	yes	yes	yes
Control of process setpoints in process controllers	no	yes	yes
Starting and stopping of control loops	no	yes	yes
Programming of local process controllers	no	no	yes
Reading of calibration data	no	no	yes
21 CFR part 11 compliant	no	no	yes
GAMP compliant	yes	yes	yes
ISA S88 standard	no	no	yes
Password protection	no	no	yes
User definable access rights	no	no	yes
Auto start after power failure	no	no	yes

Specifications

Specifications	**BioXpert Lite**	**BioXpert 2**	**BioXpert W7**
Data management			
On line data collection	yes	yes	yes
Off-line data collection	yes	yes	yes
Data storage system	Proprietary file format	Proprietary file format	SQL database
Minimum sampling frequency	1 minute	1 minute	1 second
Sample frequency selectable per parameter	no	no	yes
Data export to Excel	yes	yes	yes
Data export in ASCII format	yes	yes	yes
Graph export in BMP format	yes	yes	
On-line calculations using on-line and off-line data	no	yes	yes
Data display			
Line graphs	yes	yes	yes
Bar graphs	yes	yes	yes
Synoptic	yes	yes	yes
Procedure flow chart	no	no	yes
Combination of current and historic data in graphs	yes	yes	yes
Combination of different active batches in graphs	yes	yes	
Measured data table display	yes	yes	yes
Scatter plots	yes	yes	yes
Storage of predefined graph settings	yes	yes	yes
Supervisory control			
Programming of time based actions	no	yes	yes
Programming of event based actions	no	yes	yes
Profiling of setpoints	no	yes	yes
Manual setting of local control set points	no	yes	yes
Recipe definition	no	yes	yes
Other			
Notebook for process and equipment remarks	yes	yes	yes
Event viewer for system comments	yes	yes	yes
Audit trail	no	no	yes
Batch reports supported	no	no	yes
Remote access	no	no	yes

DO_2 Sensors

Measurements of dissolved oxygen (DO_2) in biotechnological processes is a basis for process optimization and allows to maximize the product yield. A microorganism or cell responds to the oxygen concentration in regulating its overall metabolism. Therefore the knowledge of the DO_2 concentration and the proper control during the process are of great importance. The AppliSens DO_2-sensor is specifically designed for long-term, stable and accurate measurements in bioprocesses.
The DO_2-sensor has a titanium membrane module to minimize the measurement drift. The autoclavable polarization module allows polarizing of your DO_2-sensor while autoclaving your bioreactor system, resulting in reduced start-up time for your culture.

Features

- Titanium and PEEK materials guarantees low drift
- cGMP compatible by using FDA approved materials
- Electropolished surface roughness finish of 0.4 µm eases cleaning
- Short response time
- Withstands repeated SIP and CIP cycles
- Standardized PG 13.5 connection guarantees interchangeability with other bioreactor brands

Applications

- Microbial cultures
- Cell cultures
- Batch
- Fed Batch
- Continuous cultures
- Perfusion cultures

Specifications

Optimum polarization potential	- 800 mV @ 40°C	
Polarization potential amplifier	- 675 mV	
Max. pressure where linearity is guaranteed	4 bar	
Max. sterilization temperature	135°C	
Minimum polarization time	30 minutes	
Minimum polarization time after autoclaving	4h	
Optimum polarization time after autoclaving	Overnight	
Polarization current	Air / 25 °C / 1.013 bar / 100 % RH	(33 - 66) nA
Polarization current	Air / 40 °C / 1.013 bar / 100 % RH	(65 - 98) nA
Polarization current	O_2 / 40 °C / 1.013 bar / 0 % RH	(300 - 350) nA
Response time gas phase 20 °C	t (90%)	(20 - 30) s
Response time gas phase 40 °C	t (90%)	(10 - 20) s
Response time gas phase 60 °C	t (90%)	(5 - 10) s
Drift between 15h - 5 days	< 0.2 % / day	
Drift between 5 days and 7 days	< 0.1 % / day	
Drift between 7 days and 30 days	< 0.05 % / day	
Insertion length ø 12 mm sensors:		
Z010011025	insertion length 110 mm, 215 mm total length (used with Tracfix sensor holder)	
Z010015420	insertion length 154 mm, 259 mm total length	
Z010023525	insertion length 235 mm, 340 mm total length (Bioreactor 1-5 L)	
Z010032525	insertion length 325 mm, 430 mm total length (Bioreactor 7 L)	
Z010042525	insertion length 425 mm, 530 mm total length (Bioreactor 15 L)	
Z010059025	insertion length 590 mm, 695 mm total length (Bioreactor 20 L)	
Insertion length ø 8 mm sensors:		
Z010015080	insertion length 150 mm	
Z010017080	insertion length 170 mm	

pH Sensors

In the biotech- and pharmaceutical industry it is vital to have precise information about the pH value of the bioprocess. The pH level directly affects viability, productivity, stability of the cells and it influences analysis of active ingredients.
The AppliSens pH+ sensor is specifically designed for long-term, stable and accurate measurements in bioprocesses. The pH+ sensor has a fixed sleeve diaphragm that reduces the influence of the culture medium on the pH measurement.
Compared to classic diaphragm types, the sleeve diaphragm increases measuring accuracy and increases the lifetime of the sensor which is vital for long lasting biotech cultivation processes.

Features

- Robust design by using tempered glass shaft
- Sensor head uses minimal space on bioreactor topplate
- Accurate measurement
- Low sensitivity to fouling due to sleeve diaphragm
- Stable signal over longer time
- FDA approved materials
- Withstands repeated SIP and CIP cycles
- Standardized PG 13.5 connection guarantees interchangeability with other bioreactor brands

Applications

- Microbial cultures
- Cell cultures
- Batch
- Fed Batch
- Continuous cultures
- Perfusion cultures

Specifications

Parameter	As Delivered
pH range	0 - 12 pH
Temperature range	0 - 135°C
Electrode zero point (E7)	+/-15 mV
Electrode slope (S4/7)	> 98%
Isothermal Intersection- pH (Eiso)	6.5 - 8
PH Range	4 - 9
Membrane resistance @ 25°C (ohm)	<1200
Membrane resistance @ 37°C (ohm)	<500
Calibration drift in Buffer 9 (mV / min)	< 2
Stirring Error (Buffer 9 @ 25 °C - pH)	< 0.05
Drift 72 hours after Autoclaving pH	< 0.13
Zero-point drift per week in PBS (pH)	< 0.05
Response Time (pH 9 to 4 @ 25 °C in Seconds)	< 90
Response Time 90% (pH 9 to 4 @ 25°C in Seconds)	< 45
Response Time (pH 9 to 4 @ 37°C in Seconds)	< 45
Response Time 90% (pH 9 to 4 @ 37°C in Seconds)	< 45
Insertion length ø 12 mm sensors:	
Z001012051	insertion length 120 mm, 170 mm total length (used with Tracfix sensor holder)
Z001023551	insertion length 235 mm, 285 mm total length (Bioreactor 1-5 L)
Z001032551	insertion length 325 mm, 375 mm total length (Bioreactor 7 L)
Z001042551	insertion length 425 mm, 475 mm total length (Bioreactor 15 L)
Z001059051	insertion length 590 mm, 640 mm total length (Bioreactor 20 L)
Insertion length ø 8 mm sensors:	
Z001015080	insertion length 150 mm
Z001017080	insertion length 170 mm
Sensor electrical connection	K9

pH Sensor in TracFix
retractable sensor holder

BioSenz glucose / lactate analyzer

The Applikon BioSenz is a unique measuring device specifically developed for analysing glucose and lactate in bioreactors. Patented heat-flux technology is used for continuous measurement with high precision and repeatability. The combination of the BioSenz with a process control system allows accurate control of the analyte levels in a bioreactor to optimize the performance of the bioprocess. The operation of the analyzer can be done through the process control system or via a computer using the BioSenz software.

Features

- Accurate monitoring and control of glucose and lactate in your bioprocesses
- Single-use sensor
- Compact footprint
- Stable biosensors up to 4000 measurements
- Reliability due to unique patented heat-flux measuring technology
- Connection to re-usable and single-use reactors
- Automatic calibration
- No sample preparation

Heat-flux technology

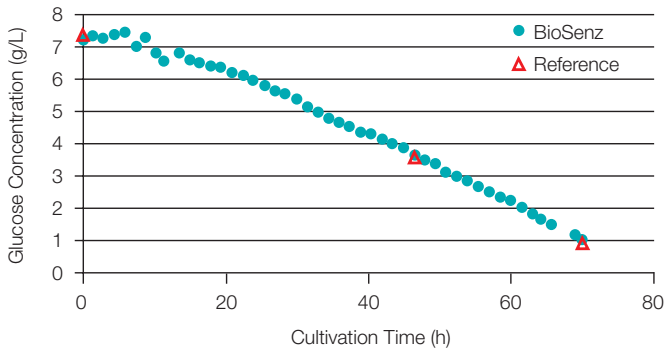
Enzymatic conversion of glucose to gluconic acid and water, or lactate to puruvate and water, which is directly proportional to the concentration of glucose in the sample. The BioSenz measures the heat-flux from the reaction, and this patented approach provides a highly accurate, highly specific determination of glucose and lactate in your bioreactor.

Concentrations measured in presence of other medium compounds in different concentrations

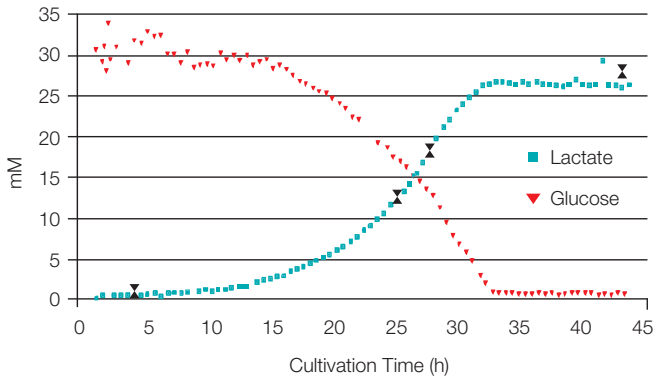
	0 mM glucose	1 mM glucose	20 mM glucose
+Fructose [2mM]	<0.3 mM	1.07 mM	19.2 mM
+Maltose [2mM]	<0.3 mM	1.04 mM	19.9 mM
+Lactose [2mM]	<0.3 mM	1.02 mM	19.5 mM
+Sucrose [2mM]	<0.3 mM	1.00 mM	19.7 mM
+Serum [2g/l]	<0.3 mM	0.96 mM	20.0 mM
+Yeast ext. [2 g/l]	-	-	19.6 mM

No interference in lactate measurement was detected by different concentrations of ascorb acid, acetaminophen (paracetamol) and uric acid.

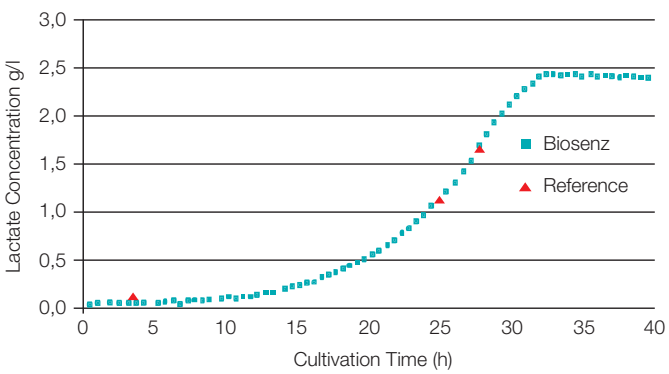
Batch Cell Culture Analysis



Lactate and Glucose | L. Plantarium Fermentation



Cell Culture with Glucose Feeding



System setup

The sterilizable and autoclavable sample probe is used to take a cell-free sample from the bioreactor. The system has integrated buffer solutions and calibration standards to minimize the footprint. The auto-calibration function reduces operator involvement and increases the reliability of the measurements. The optional multiplexer allows the system to be connected to up to four bioreactors simultaneously. Analog outputs are used to connect the analyzer to a process control system. The sensor chip determines the analyte to be measured. At the moment we offer glucose and lactate analysis.

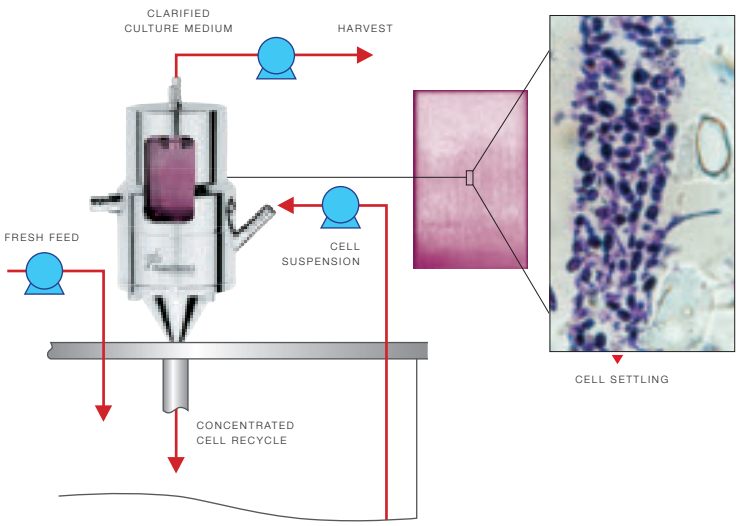
Technical data

	Glucose	Lactate
Measurement principle	Enzymatic heatflux	
Measurement range (g/l)	0.05 - 8	0.05 – 2.5
Measurement deviation	<3%	<3%
Measurement frequency	Up to 10 per hour	
Active sensor life	30 days or >4000 samples	
Sensor shelf life	>6 months (at 2 – 8 °C)	
Communication interface	USB and analog output (option)	
Maximum number reactors per analyzer	Up to 4 with optional Multiplexer	
Dimensions (HxWxD)	33 x 15 x 36 cm / 13 x 6 x 14“	
Weight (kg)	6.5	

BioSep, acoustic cell retention system

The Applikon BioSep system is a unique, cell retention device for high-density perfusion processes. Using high frequency resonant ultrasonic waves to separate cells instead of a physical mesh or membrane, it offers all the benefits of traditional devices but without their inherent problems and limitations. The BioSep, based on the technology of acoustic resonance, is a non fouling / non clogging retention system. The BioSep can be applied in both R&D (max. 1 L/day), process development and on production scale (1000 L/day).

Typical configuration of acoustic cell retention system



Features

- Proven under cGMP conditions
- Easy to install and to operate
- Can be used in combination with any brand of bioreactor
- Long term cultivation possible (> 6 months)
- No fouling or blocking
- No damage to the cells
- High separation efficiency (> 95%)

Applications

- Cell cultures
- Perfusion cultures.

Specifications

BioSep system	**1L**	**10L**	**50L**	**200L**	**1000L**
Maximum perfusion rate	1 L/day	7 L/day	45 L/day	200 L/day	1000 L/day
Minimum perfusion rate	0.1 L/day	0.7 L/day	4.5 L/day	20 L/day	100 L/day
Separation efficiency	Up to 99% (depending on cell concentration and perfusion flow)				
Minimum cell concentration	2 x 10^5 cells/ml (depending on cell size)				
Bioreactor connection	6 mm OD tube	12 mm OD tube	Mounted separately	Mounted separately	Mounted separately
Medium inlet	3 mm hosebarb	6 mm hosebarb	10 mm hosebarb	0.5” TC	0.5” TC
Return line to bioreactor	3 mm hosebarb	6 mm OD diptube	0.5” TC	0.5” TC	0.5” TC
Perfusion outlet	3 mm hosebarb	6 mm hosebarb	6 mm hosebarb	0.5” TC	0.5” TC
Weight	0.1 kg	0.5 kg	1.5 kg	13 kg	70 kg
Resonator volume	0.7 ml	7 ml	50 ml	290 ml	1450 ml

BioSep Controller	**APS 995**	**APS 990**	**APS 990**	**APS 992**	**APS 993**
BioSep Controller Power	15 Watt	150 Watt	150 Watt	350 Watt	1500 Watt
BioSep Controller Dimensions (DxWxH, mm)	Combined with my-Control	305x130x130	305x130x130	450x400x135	450x300x450
BioSep Controller Weight (kg)	Combined with my-Control	3.5	3.5	17.6	43

Bench scale and Pilot plant steam-in-place bioreactor systems

Applikon's concept of modularity (using standard modules to customize the functions of the bioreactor) is extended to the stainless steel pilot plant bioreactors as well. For scale up purposes the range of the Bio Bench and Pilot Systems, designed and built to the latest standards on hygienic processing and cGMP and GAMP validation requirements, complements the laboratory scale bioreactor systems. Scale-up from laboratory scale to pilot plant and small scale production is simplified by the consistent bioreactor design and the scalable control solutions. All systems are designed to be cleaned-in-place. Applikon offers CIP systems ranging from fully manual control to fully automated. Standardized bioreactor systems are available up to 140 liter total volume and custom build units can be supplied up to 2,000 liter total volume.

Features

- Easy to clean mirror polished external finish
- Electropolished finish of all parts in contact with the culture (Ra < 0.4 µm) to allow efficient clean-in-place
- Modular design allows easy adaptation to changing process demands
- Magnetically coupled agitator for peace of mind
- cGMP compliant design simplifies validation
- Compact design reduces floor space needed
- Open frame construction gives easy access for maintenance and operation

Applications

- Scale-up studies
- Medium optimization
- Process optimization
- Small scale production
- Microbial and Cell culture
- Batch, Fed-Batch, Perfusion and Continuous cultivation

15 Liter BioBench with ez-Control

Specifications

	Total volume (liter)	Working volume (liter)	Minimum working volume (liter)	Aspect ratio total volume	Aspect ratio working volume
7 liter Bio Bench	7	5	2	2.2	1.5
15 liter Bio Bench	15	10	4	2.1	1.4
20 liter Bio Bench	20	15	4	3.0	2.2
30 liter Bio Bench	30	22.5	7	2.0	1.6
30 liter Pilot Cell	30	20	7.5	1.5	1.0
60 liter Pilot Cell	60	40	10	1.5	1.0
130 liter Pilot Cell	130	100	28	1.5	1.0
20 liter Pilot Microbial	20	15	4	3.0	2.2
40 liter Pilot Microbial	40	30	7.5	3.0	2.2
70 liter Pilot Microbial	70	50	10	3.0	2.2
140 liter Pilot Microbial	140	100	20	3.0	2.2
Custom build bioreactor systems are available up to 2000 liter total volume					
Drive system	Magnetically coupled, optional mechanical seal, bottom or top mounted agitator for microbial cultures and top mounted for cell cultere systems				
Maximum agitator tipspeed (m/s)	5 m/s for microbial cultures and 1 m/s for cell cultures				
Impellers	Rushton and marine with outside diameters 0.33 - 0.5 vessel diameter				
Gas sparger	Porous sparger, L-Sparger or Ring-type sparger				
Gas overlay	Optional gas overlay line				
Exhaust gas	Water cooled exhaust gas condenser with internal spiral and/or jacketed				
Sampling	Optional resterilizable sample system in DN25 port in lower side wall				
Draining	Resterilizable bottom mounted bellows drain				
Additions	Sterilizable additions (push valves) and resterilizable addition ports				
pH	Measurement: 12 mm classic pH sensor in DN25 port in lower side wall				
	Control: via acid pump or CO_2 gas (rotameter or MFC) in combination with alkali pump				
DO_2	Measurement: 12 mm polarographic DO_2 sensor in DN25 port in lower side wall				
	Control: via a combination of N2, Air, O_2 (Rotameter or MFC) and agitation or nutrient addition pump				
Temperature	Measurement: Pt-100 sensor in in DN25 port in lower side wall				
	Cultivation control: cooling and heating jacket via bioreactor wall				
Foam	Measurement: Height adjustable conductivity based foam sensor				
	Control: Anti foam addition pump				
Level	Measurement: Height adjustable conductivity based level sensor or loadcells in bioreactor frame				
	Control: pump for liquid addition or removal				

Special projects, customized solutions

Some customer demands cannot be fulfilled with our standard product offerings. In these cases we build custom solutions for our customers. These projects can range from very special mini bioreactors to a complete line of cGMP production systems ranging up to several thousand liters volume systems.

1500 Liter Bioreactor with i-Control

Key to the success of these projects is our experience of over 35 years building customized bioreactor solutions in combination with clear communication between our project team and the customer. We have developed special web based tools for communication and open information exchange within the project team. This ensures that everybody is working with the same up-to-date information all the time. The result of this approach is a customized bioreactor system that is delivered on time and completely according to the customer's specifications.

Over the past years we have generated a large library of customized solutions for a variety of specific demands. This guarantees that we can supply our customers with a proven solution for virtually any process demand.
Since we are standardized on supplying products for the pharmaceutical industry, all our products and processes are fully documented. Our ISO 9001 certificate underlines the high quality level of our work and accompanying documentation.

AppliCare, total process control

What separates our service engineers from other organizations is that our people are BioProcessing Specialists. This means that not only do we know how to maintain and repair equipment, we can also troubleshoot because we understand process control. We specialize in bioreactors, controllers, software, motors, probes and all phases of your specific system's operation. Applikon's AppliCare will fix your problems - guaranteed. We help to eliminate the lost hours incurred to your production schedule and the high costs of downtime.

Installation and training

A correctly installed system, with comprehensive on-site training minimizes set-up time and ensures optimum operation within the shortest timeframe.
The installation service incorporates:

- Pre-plan design & Supply Service Requirement over-view before arrival of Applikon Equipment into your lab
- Connection of all tubing. hoses or piping from the Applikon Control Skid to the Supply Services or the Utility Panels
- Installation of all cabling from SCADA software to the controllers
- Site acceptance tests

Preventive maintenance

Downtime and emergency call-outs can be costly and always happen unexpectedly during an important run. Preventive maintenance extends the lifetime of the major components of your system, preventing premature wear and failure.
Benefits of Applikon's service agreements:

- Reduced charges for emergency repairs
- Free access to firmware upgrades
- Reduced labour charges for any upgrade work or refresher training on site.

Extended warranty

This plan is a two-year extension of the original equipment warranty,
and includes parts and labor as needed.
Instrument calibration service

- Validation
- Calibration certification

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